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Review Article

Up In The Air With Diabetes: A Systematic Review of Literature and A Pragmatic Approach to Diabetes Management During Long-Distance Travel

Gagan Priya[1]*, Sanjay Kalra[2], Deep Dutta[3], Emmy Grewal[4], Indira Maisnam[5] and Sameer Aggarwal[6]

[1]*Department of Endocrinology, Fortis & Ivy Hospitals, Mohali, Punjab, India*

[2]*Department of Endocrinology, Bharti Hospital, Karnal, Haryana, India*

[3]*Director, CEDAR Super-specialty Center, New Delhi, India*

[4]*Department of Endocrinology, Max Hospital, Mohali, Punjab, India*

[5]*Department of Endocrinology, RG Kar Medical College, Kolkata, West Bengal, India*

[6]*Department of Endocrinology, Apex Hospital, Rohtak, Haryana, India*

Abstract

Introduction

Long-distance travel by air has become immensely popular in modern times, but for the person with diabetes, it creates unique challenges including transportation of insulin and other supplies, performance of glucose-monitoring and insulin delivery devices within the aircraft, adaptation to new time zones and altered lifestyle, and titration of medications. There are no published guidelines for the management of diabetes in travelers.

Methods

We conducted a search of Pubmed and MEDLINE using keywords 'diabetes', 'insulin', 'insulin pump', 'CSII', 'glucometer', 'continuous glucose monitoring', 'CGM', 'travel' and 'air travel' for publications between Jan 1980 to 22nd Feb 2020. We found 56 relevant publications, but most were either narrative reviews or observational studies describing challenges in management of diabetes during travel.

Discussion

Individuals with diabetes should be counselled about the need for pre-travel evaluation and carrying adequate stock of medications, insulin and glucometer supplies much in excess of the planned duration of stay. Care should be taken to maintain cold chain during travel and insulin should be carried in hand-bag only as it may be exposed to freezing temperatures in checked-in bags. During security, insulin pumps and continuous glucose monitoring devices should not be put through the scanner but manually inspected. When traveling east, the day is shortened while it is lengthened when going west. This would require appropriate adjustment of insulin doses guided by capillary blood glucose monitoring.

Conclusion

Safe flying with diabetes is all about planning ahead, packing adequate supplies, maintenance of cold chain for insulin, frequent monitoring of blood glucose and titration of medications as well as insulin, and minimizing the risk of hypoglycemia or hyperglycemia.

Keywords: Air travel; Diabetes; Insulin; Insulin Pump; Long-distance travel; Type 1 diabetes

Introduction

Air travel has become an immensely popular mode of transportation in modern times, connecting almost every corner of the globe. Common reasons for travel include business, study, family visits, pilgrimage and vacations over varied lengths of stay from few days to several months. There has been a steady increase in the number of travelers worldwide, including people with chronic diseases like diabetes, hypertension and cardiovascular disease, who need extra care during travel. The travel clinic of Public Health Service in Amsterdam reported a significant increase in the number of travelers with diabetes between 2001 to 2011 [1].

Quite often, people fly across continents and oceans, spanning several time zones. Long-distance travel is considered as travel across ≥5 time zones. The day is shortened when traveling eastward and lengthened when going west. This results in a need to adapt to the new time zone with respect to meal timings, lifestyle and activity, as well as sleep schedule. In addition, during long-hauls, crossing time zones is likely to change the interval between insulin and medication doses (shorter intervals going east, longer going west). There is also a need to carry adequate medications and related supplies depending on the intended length of stay. In addition, the traveler has to navigate airport security and aircrafts are hypobaric (low-pressure) cabins. This creates challenges with insulin transportation and storage as well performance of glucose-monitoring and insulin delivery devices.

There exist no guidelines for the management of diabetes during travel. This leaves diabetes care providers with little guidance on how to address travel-related queries. Some patient guidance is available

***Corresponding author:** Gagan Priya, Department of Endocrinology, Fortis & Ivy Hospitals, Flat 104, Marigold Tower, Mayfair Apartments, Sector 70, Mohali, Punjab, India- 160071, Tel: +91 9878607939; E-mail: gpriya77@gmail.com

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through health and travel magazines but the advice is not well-structured. Diabetes U.K. provides general tips for travelers with diabetes which may be helpful [2].

In this systematic review, we review the current literature pertaining to travel in individuals with diabetes and offer solutions for various challenges they faces when traveling over long-distances by air.

Methods

We conducted a search of Pubmed and MEDLINE using keywords 'diabetes', 'insulin', 'insulin pump', 'continuous subcutaneous insulin infusion', 'CSII', 'glucometer', 'continuous glucose monitoring', 'CGM', 'travel' and 'air travel' for publications between Jan 1980 to 22nd Feb 2020.We restricted the search to articles in English. The search revealed over 1500 publications, of which only 56 were found relevant. Of these, 18 publications provided general travel tips for individuals with diabetes [3-20].

One observational study [21] evaluated the adequacy of pre-travel counseling and change in glycemic control during travel in individuals with type 2 diabetes when traveling abroad, while two others included patients of both type 1 and type 2 diabetes [22,23] Pinsker et al. [24], Driesser et al. [25] and Levy-Shraga et al [26] reported surveys of individuals with type 1 diabetes with focus on travel-related concerns and glycemic fluctuations.

In one survey of British South Asians who visited east, authors reported on changes in healthcare behavior [27]. In a case report from Japan, Kishimoto et al highlighted the issue of language and lifestyle barriers as well as inadequate healthcare insurance as hurdles to diabetes care in foreign visitors [28]. 5 articles focused on travel in Hajj pilgrims with diabetes, 3 of these were narrative reviews [29-31] while 2 observational studies reported on foot ailments [32,33].

Many publications were narrative reviews and were based on expert opinion [34-44]. One narrative review discussed issues related to airline security [45]. The review by MacNeill et al was focused on travel recommendations for insulin pump users [36]. Three narrative reviews discussed issues related to diabetes and trekking, especially at high altitudes [41,46-47], Sane et al. [48] and Chandran et al. [49] provided practical suggestions with regards to insulin dose titration while traveling based on individual experience and case reports.

Olateju et al. [50], deMol et al. [51] and Fink et al. [52] assessed the effect of altitude on the performance of glucometers, while the effect of altitude on glucose sensors was reported by Adolfsson et al. [53]. One study evaluated the effect of altitude on insulin delivery from insulin pumps [54], Pavela et al. published a systematic review of current recommendations on diabetes care during travel in 2018 [55].

The challenge

Individuals with diabetes face several important challenges during travel, as enlisted in Table 1. An important dilemma for people taking insulin relates to transportation and administration of insulin during travel, especially when traveling across various time zones. The dilemma also extends to newer devices of glucose monitoring such as continuous glucose monitoring (CGM) and insulin delivery devices including insulin pens and continuous subcutaneous insulin infusion (CSII).

	Challenges and concerns
Before travel	Pre-travel evaluation Need for complete updated prescription Gather and pack supplies - medications, insulin, glucometer, glucose tablets or candies, snacks
Security and customs	Need to declare medications Insulin, pens, syringes, glucometer and lancets need inspection Longer time – may need pat down and extra inspection Insulin pump – not to put under scanner CGM device – not to put under scanner
In flight concerns	Longer days when flying west, shorter days when traveling east Change in meal timing – need to adjust insulin and medication dose Altered sleep pattern Risk of hypoglycemia or hyperglycemia Risk of deep vein thrombosis Erratic delivery of insulin from pump while take-off or landing Errors in glucometers or CGM at high altitudes Other medical emergencies – cardiovascular, respiratory
During stay abroad	Altered lifestyle – meal times, meal composition and activity levels Jet lag and altered sleep patterns Risk of hypoglycemia or hyperglycemia Risk of running out of supplies Inter-current illness, infections, foot injury Lack of adequate health insurance Lack of knowledge about how to navigate medical emergencies abroad

Table 1: Challenges in individuals with diabetes during international travel.

While short-distance travel may not interfere with daily routine, long-distance travel may lead to altered meal-timings, day-night schedule, limited and different food choices and limited physical activity. Vacations are further associated with change in dietary patterns and composition and activity levels that can affect glycemic control. Those traveling abroad may also be unable to procure supplies in a different country. This is an important challenge that many elderly people face when visiting their children abroad. They may often go for prolonged periods of time from 3 to 6 months, even beyond 1 year with "super-visas". These issues have been highlighted in several retrospective surveys, which also noted that travel-related advice from healthcare providers was often inadequate.

In a survey of 493 people with diabetes taking insulin, 44% had traveled within the last 12 months. 10% experienced hypoglycemia during travel or within the first 24 hours of arrival. Most individuals wished they were provided more information about travel [23]. In a recent study, 65 men and 74 women with type 2 diabetes were assessed through a self-administered questionnaire. 8.6% reported hypoglycemia during travel and these episodes were related to the number of time zones crossed. Less than one-fourth subjects sought travel advice. In addition, most physicians did not offer pre-travel counseling even after travel plan was mentioned [21].

In a retrospective questionnaire-based study of 533 members of the Type 1 Diabetes Exchange online community, 71% had flown across long distances in the past 5 years. CSII users (with or without CGM) reported that their biggest fear was losing supplies during travel, while those not on CSII were worried about glucose fluctuations. 9% avoided international travel due to their diabetes. 74% reported that hypoglycemia and/or hyperglycemia had increased when traveling overseas. 22% ran out of supplies. Specific issues in knowledge and resources related to navigating airport security, managing insulin and emergency management [24].

Another observational survey of 19 travelers with diabetes on insulin visiting tropical countries reported that 55% had more glycemic fluctuations during travel. 5 patients had difficulty in adjusting insulin doses [25]. In a retrospective study that compared 47 young type 1 diabetics with controls during international trips in the last 5 years, diabetics sought travel advice prior to 71% trips, increased glucose monitoring during 41% trips and reported worsened glycemic control during 11% trips. The incidence of travel-related diseases such as fever or diarrhea was not increased [26]. In a survey of 44 British South Asians who traveled east for holidays, Patel et al identified several barriers to care including altered lifestyle and reduced adherence to medications [27].

Gill et al surveyed diabetes care providers in UK, asking for what advice they would give to fliers using short or intermediate-acting insulin going east or west. 37% responses were found inadequate and non-uniform. 13% responses were likely to cause hypoglycemia [22]. Air travel is associated with exposure to low cabin pressures. The ambient pressure at sea level is 760mmHg. In airplanes, cabin pressure is approximately 200mmHg lower, mimicking the pressure at approximately 8,000 feet. This can affect performance of glucose-measuring and insulin-delivery devices [50,51,53,54]. While interventional studies are difficult to conduct, there is a lack of adequate studies on device performance during air travel.

Planning a head

Air travel is considered safe for individuals with diabetes. However, pre-travel evaluation and stabilization of metabolic control is highly advisable. Advance planning can go a long way in minimizing problems and emergencies.

Quite often, the travelers defer their clinic visits to the last possible moment, leaving very little opportunity to titrate medication and optimize control. Good practice would be to discuss travel plans with healthcare provider at least 1-2 months in advance, so that metabolic control is optimized. This would also allow for evaluation of complication status and implementation of appropriate therapy [49].

It has been suggested that 'unstable proliferative diabetic retinopathy' may worsen as air crafts have a relatively hypoxic environment. Therefore, appropriate redressal of retinopathy should be considered before travel [55]. Foot assessment and reinforcement of foot care is warranted, especially in those who are likely to engage in walking, trekking or hiking or pilgrims who may be walking barefoot.

At cruising altitudes of approximately 29,000-39,000 feet, airlines usually maintain cabin pressure of 7,800-8,000 feet; at this high altitude, the arterial partial pressure of oxygen decreases from 98mmHg to approximately 60-70mmHg. This may create issues related to hypoxia in individuals with decompensated cardiovascular or pulmonary disorders and fitness to travel needs to be assessed in pre-travel visit. An arterial blood gas may be useful in such high-risk patients [40].

Many people opt for travel health insurance for emergencies. The individual should be instructed to enquire about the sort of healthcare facilities and accessibility to the same at the destination in advance [55]. In case of prolonged travel, it would be good practice to find out from where medical supplies can be procured at the destination in case of any issues [2].

Meals can be pre-booked on most flights and the individual can choose from different meal options including specific meals for diabetes, low-calorie meals, low fat meals, etc. Individuals with type 1 diabetes with concomitant celiac disease can pre-book gluten-free meals.

Packing supplies

Table 2 provides a checklist of supplies that individuals with diabetes should pack before travel. They should be instructed to carry complete, clear and recent prescription from their healthcare provider for medications, insulin and other relevant supplies. This would ease transit through security and customs and would also provide medical details in case of any unforeseen emergency abroad. The name on the prescription should match the one on the ticket and passport.

Category	What to pack
Medications	In surplus of the amount required to cover the duration of stay • Oral antidiabetics • Other injectable antidiabetics (only in hand-bag) • Other prescription medications including antihypertensives, statins, aspirin, etc. • Medications for nausea, vomiting, diarrhea, fever • First aid kit Can be split between hand-bag and checked-in bags.
Insulin and related supplies	In surplus of the amount required to cover the duration of stay • Insulin vials, cartridges and pens (only in hand-bag) • Spare insulin pen (in hand-bag) • Syringes and needles
Glucometer and CGM devices	In surplus of the amount required to cover the duration of stay • Glucometer including one spare glucometer • Spare batteries • Glucometer strips • Lancet needles • CGM supplies with spare glucometer • Urine ketone strips (for those with type 1 diabetes)
Insulin pump	• Pump worn as such on person • All pump supplies including insulin cartridges, tubing, etc. in surplus of the amount required to cover the duration of stay • Extra supplies of insulin pens with needles including both rapid and long-acting insulin for use in case of pump malfunction
Hypoglycemia care	• Glucose tablets, gels, candies or liquid drinks • Glucagon kit in those at high risk of hypoglycemia or hypoglycemia unawareness • Complex carbohydrate-containing snacks (cereal bars, cookies, nuts, cheese crakcers, etc.)
Documents	• Complete, legible and recent prescription including complete diagnosis and medication list • Insurance documents • Medical identity document (ID)
Footwear	• Comfortable fitting footwear • Absorbent socks

Table 2: What to pack before embarking on travel?

The Transport Security Administration (TSA) in US along with American Diabetes Association (ADA) provides information about carrying medications and insulin supplies [56]. TSA advises that medications, insulin, needles or syringes, glucometer, glucometer strips and lancets should be carried in their original packing with proper labeling. Lancet needles can be carried in hand-bag but should be

capped and carried in original packing along with glucometer. Gel packs can be carried for insulin cold chain. Medications and supplies are best packed in a separate clear bag so that they can be quickly taken out for inspection.

It is advisable to pack surplus supplies of medications, almost double the amount required for the duration of stay to avoid issues in case of prolonged stay or problems related to break in vials or cartridges [49]. While half the supplies can be put in checked-in baggage, enough should be kept in handbag in the event of lost baggage. Supplies can also be split between checked-in bags. However, insulin vials, cartridges and pens and glucometer and glucometer strips should be kept in hand-bag only as they may be exposed to freezing temperature in checked-in bags [40]. Non-insulin injectable anti-diabetes medications such as glucagon-like polypeptide-1 receptor agonists (GLP-1RA) and glucagon kit should also be carried in hand-bag. In case any of these supplies are put in checked-in bags, insulin needs to be properly insulated and examined before use for crystals or cloudiness.

In addition, glucose tablets, gels or candies and snacks must be packed for use in the event of hypoglycemia. The TSA allows liquids (such as juices) in excess of 100 ml for individuals with diabetes and they can be carried through security after inspection [56]. However, this may differ in other countries and the individual needs to inquire about specific regulations.

Passing through airport security and customs

All insulin vials, cartridges and pens need to be taken in hand-bag. This would ensure the maintenance of cold chain, make insulin easily accessible while in the aircraft and also minimize the chances of loss in transit. All diabetes-related supplies including medications, devices, and liquids are admissible through airport security since 2016 [34]. The security staff should be informed about diabetes supplies when security check begins.

Insulin vials, cartridges and pens can be put through the X-ray screening machines. However, insulin pumps and CGM devices may be affected by body scanners and X-ray machines. While some manufacturers suggest that insulin pumps can be safely checked with metal detectors but not X-ray machines [57] specific manufacturer guidelines should be followed. Most manufacturers advise to avoid going through body scanners with the pump. The individual is advised to continue wearing the device (pump and/or CGM) and request a manual pat-down with inspection of the device. Alternatively, the device can be disconnected and inspected but not put through the scanner [56]. Security check may take extra time; therefore, sufficient time should be kept to avoid undue stress.

Device performance in flight

Aircrafts fly at high altitudes and are low-pressure (hypobaric) cabins. This can affect the performance of devices.

Glucometers: Some studies have raised doubts over the accuracy of glucometers at high altitudes in low-pressure cabins. Glucose oxidase and glucose dehydrogenase (GDH)-based meters may overestimate glucose values, though GDH meters are more accurate. Fink et al compared 7 commonly used glucometers during mountaineering; glucometer performance was affected by elevation, temperature and relative humidity and glucometers underestimated glucose levels at high altitudes [52]. However, others have suggested that the margin of error is small and they can be relied on for decision-making [50,51].

Continuous glucose monitoring devices: In a small study with CGM under hypobaric conditions, input signals for glucose significantly varied at low and high glucose concentrations [53]. Therefore, it would be advisable to validate CGM readings as it may not only lead to erroneous reading of glucose, but also affect the performance of CGM-integrated pumps.

Insulin pens: Pen devices continue to function well at high altitudes. However, needles should be removed after injection as changes in air pressure during ascent and descent can cause entry of air bubbles and expulsion of insulin.

Insulin pumps: There are concerns about accuracy of insulin delivery through pumps at high altitudes. During ascent, formation of bubbles in the reservoir may lead to inadvertent delivery of insulin and risk of hypoglycemia [54]. Higher the insulin volume, greater is the likely displacement of insulin. Therefore, it would be useful to fill the reservoir with only 1.5ml insulin. Some pump monographs suggest that pump should be disconnected during take-off and landing. [55]. Once at cruising altitude, the reservoir is taken out and any air bubbles from the tubing removed before reconnecting. During landing also, pump is disconnected, and the tubing primed with 2 units insulin before reconnecting. [54]. However, studies with modern pumps suggest the chances of inadvertent insulin delivery are very low.

Titration of non-insulin therapies during travel

There exist no guidelines on dose titration of medications during travel. Most individuals can continue to take prescribed medications in previous doses. The timing of medication needs to be adjusted as per change in time zones. When traveling east or if a meal is skipped during travel, one dose of oral anti-diabetic (especially insulin secretagogues) can be skipped and dose then adapted to new time zone [55]. Medications with low risk of hypoglycemia (such as metformin, dipeptidyl peptidase-4 inhibitors, sodium glucose co-transport-2 inhibitors, GLP1-RAs, or thiazolidinediones) can be continued as such and switched to new time zone on arrival. It is important for travelers not to skip meals and maintain consistent meal patterns during travel to avoid hypoglycemia.

Titration of insulin during travel

When spanning time zones, changes in insulin dose are often needed based on alterations in day-night cycles. The alteration is likely to be minimal when ≤2 time zones are crossed and time difference in <3 hours, but increases with increasing number of time zones crossed. The 2004 ADA Guidelines recommend that doses must be adjusted when a person is crossing ≥3 time zones but does not address how. [58]. Till now, no guidelines exist with regard to insulin dose adjustment during travel. Some authors have provided guidance on adjustment of insulin doses based on clinical experience [37,48,55].

The usual tendency is to take lower insulin doses to avoid hypoglycemia, but some may take higher doses. Many patients may be injecting a higher than required basal insulin, increasing risk of hypoglycemia. On the other hand, prandial insulin doses maybe insufficient exposing them to postprandial hyperglycemia. In one study, 10% travelers developed hypoglycemia during travel or in the first 24 hours of reaching their destination. 31% of these were episodes of severe hypoglycemia [23].

While bolus insulin can be adjusted based on SMBG and carbohydrate counting as usual, confusion remains regarding adjustment and timing of basal insulin, especially when traveling across time zones [37,48]. The day is lengthened when traveling west and may involve an extra meal. This may be covered by an extra dose of bolus insulin. In case of premixed insulin, half of the dose can be taken with extra meal and then insulin regimen switched to the new time zone upon arrival. [37,55]. On the other hand, when going east, the day is shortened. If the change in >2 hours, the amount of basal insulin may need to be decreased. The dose of basal or premixed insulin taken during travel can be reduced by half and then previous dose schedule followed on arrival. [48,55].

In table 3 we discuss insulin dose modification in a hypothetical scenario of a person with diabetes traveling west. In table 4 we discuss insulin dose modification in the same person when returning from west to east.

Scenario: Person traveling from New Delhi to Toronto	
• A person with diabetes boards a flight from New Delhi to Toronto (non-stop). • Departure time: 00:05, New Delhi (time at destination port, i.e. Toronto – 13:35) • Arrival time: 6:05, Toronto (time at departure port, i.e. New Delhi – 16:35) • Flying time – 15 hours 30 minutes • Time zone difference: 10 hours 30 minutes (gain)	
Scenario 1: Basal bolus insulin regimen He is on insulin glargine 16 units once daily at 10 pm and insulin as part 6 units with each meal.	• He will take dinner before boarding at 20:00 (New Delhi time), at which time pre-dinner dose of insulin as part can be taken as such. • Insulin glargine can be administered as scheduled at 22:00 (New Delhi time). • In flight, meal will be served approximately 1 hour into the flight. This can be covered with insulin as part as required (2-3 units, guided by capillary blood glucose). • Around 6-7 hours into flight, next meal will be served – patient can take a bolus dose of insulin as part (4-6 units, guided by capillary blood glucose). • The next meal will be served around 13-14 hours into flight – this can be covered with insulin as part (4-6 units, guided by capillary blood glucose). • Upon arrival at Toronto in early morning, patient can take his usual breakfast dose of insulin as part with breakfast and can take his insulin glargine between 10:00-12:00, Toronto time (that corresponds to 10 pm, New Delhi time), without changing the interval between glargine doses significantly. • If the person is taking insulin degludec as basal, he can take degludec at 22:00, Toronto time (which would be approximately 34-35 hours after last dose) as degludec offers flexibility in dose timing of 8-40 hours.
Scenario 2: Premix insulin regimen He is on premix as part (30/70) 16 units before breakfast and 12 units before dinner.	• He will take dinner before boarding at 20:00 (New Delhi time), at which time pre-dinner dose of premix insulin (12 units) can be taken as such. • In flight, meal will be served approximately 1 hour into the flight. No dose is administered. • Around 6-7 hours into flight, next meal will be served – patient can take half the dinner dose of premix insulin (6 units), guided by capillary blood glucose. • The next meal will be served around 12-13 hours into flight shortly before arrival – dose can be skipped. • Upon arrival at Toronto in early morning, patient can take his usual breakfast dose of premix insulin (16 units) with breakfast.

Table 3: Insulin dose modification in a person with diabetes traveling west.

Person traveling from Toronto to New Delhi	
• A person with diabetes boards a flight from Toronto to New Delhi (non-stop). • Departure time: 22:10, Toronto (time at destination port, i.e. New Delhi – 8:40) • Arrival time: 21:35, New Delhi (time at departure port, i.e. Toronto – 11:05) • Flying time – 13 hours 55 minutes • Time zone difference: 10 hours 30 minutes (loss)	
Scenario 1: Basal bolus insulin regimen He is taking insulin glargine 16 units once daily at 10 pm and insulin as part 6 units with each meal.	• He will take light dinner before boarding at 19:00 (Toronto time), at which time insulin dose can be omitted. Basal dose was taken in the morning. • In flight, meal will be served approximately 1 hour into the flight. This can be covered with dinner dose of insulin as part (4-6 units, guided by capillary blood glucose). • Around 6 hours into flight, next meal will be served – patient can take a bolus dose of insulin as part (4-5 units, guided by capillary blood glucose). • The next meal will be served around 12-13 hours into flight – can be covered by small dose of insulin aspart (4-6 units, guided by capillary blood glucose). • Upon arrival in New Delhi, he can take his usual dose of glargine between 22:00-23:00, New Delhi time (without changing the interval between glargine doses). • If the person is on insulin degludec (instead of glargine) and is taking it at 22:00 Toronto time, he can take it after take-off from Toronto. The next dose can be at 22:00, New Delhi time (which would be approximately 12 hours since last dose) as degludec offers flexibility in dose timings of 8-40 hours.
Scenario 2: Premix insulin regimen He is taking premix as part (30/70) 16 units before breakfast and 12 units before dinner.	• He will take light dinner before boarding at 19:00 (Toronto time), at which time he can skip insulin. • In flight, meal will be served approximately 1 hour into the flight. This can be covered with dinner dose of premix insulin (12 units). • Around 6-7 hours into flight, next meal will be served – he can half the breakfast dose (8 units). • The next meal will be served around 12 hours into flight shortly before arrival – he can take his dinner dose of premix insulin (12 units) and switch to his usual schedule from next morning.

Table 4: Insulin dose modification in a person with diabetes traveling east.

Insulin analogs score some advantages over conventional insulin in travelers – rapid-acting analogs have lower risk of hypoglycemia, better postprandial glycemic control and can be administered immediately before or after meal; basal analogs offer less glycemic variability and lower risk of hypoglycemia. Ultra-long acting insulins such as degludec and glargine U-300 have a significantly longer duration of action and offer flexibility; they can be adjusted to a suitable time of the day according to convenience, without much change in glucose-lowering effect or risk of hypoglycemia [35]. Insulin dose modifications need to be individualized. While transient hyperglycemia is acceptable, hypoglycemia is best avoided. There may occur unpredictable changes in insulin sensitivity with day and night shifts. The timing of the dawn phenomenon may shift; meal timings are likely to change and so are activity levels [42].

Insulin pump adjustments

An important question is the adjustment of pump clocks to local time zones. During travel, lower rates of temporary basal can be considered to avoid hypoglycemia, especially during long flights. The pump clock is then adjusted to local time on arrival and basal rates continued as such [55]. Bolus doses can be adjusted using frequent SMBG or CGM and carbohydrate counting. CGM-based data may help provide some insight into how best to adjust insulin regimens. In the absence of CGM, frequent SMBG is required.

A back-up plan of insulin pens or syringes should always be maintained in place in the event of pump malfunction. Individuals should carry additional basal insulin along with rapid-acting insulin, in case of pump failure [34].

Managing diabetes upon arrival

On arrival, meals and medications can be switched to local time.It is important to monitor blood glucose regularly both during the journey and during stay abroad.Clear written instructions on insulin titration for dose adjustments based on SMBG can be of great assistance. Several studies have shown that in general outpatient care, insulin can be successfully titrated by individuals using information from SMBG [59-61]. While there are no studies of self-titration algorithms in travelers, they are likely to improve patient self-confidence and glycemic control.

Upon arrival, care should be taken to store insulin at appropriate temperature and avoid exposure to heat. Insulin should not be left in the car glove compartment [62]. Sharps such as syringes, needles and lancets should be stored in sharps containers and local guidelines should be followed for safe disposal [62].

While individuals should carry adequate supplies, sometimes these may need to be procured at the destination. It is important to educate individuals that different glucometers have different measuring units, so that errors in interpretation of readings are avoided. For glucose, 1mmol/L is equivalent to 18mg/dl. In case insulin syringes are procured abroad, care is needed to ensure that the units on the syringe match the ones on the vial to avoid dosing errors; U-40 syringe should be used for 40U/ml vials and U-100 syringe for 100U/ml vial. Insulin pens overcome this potential pitfall. But pens may malfunction and a spare pen should always be kept.

Hypoglycemia care during travel

It is important to reemphasize about the prevention, early recognition and management of hypoglycemia. Travelers with diabetes should be instructed to carry supplies of glucose tablets, gels or liquids along with carbohydrate-containing snacks at all times. Intramuscular glucagon kits are very useful in those on insulin, especially individuals with type 1 diabetes or those at high risk of hypoglycemia and hypoglycemia unawareness [41]. Insulin doses should be guided by more frequent SMBG. It is better to err on the side of mild hyperglycemia. Those who are traveling alone should intimate airline staff of their condition and use of insulin, so that appropriate action can be taken in the event of hypoglycemia. Medical ID is also useful in such scenario.

There is lack of data about the frequency of hypoglycemia episodes reported as 'in-flight emergencies' and many such episodes probably go unreported. However, syncope was the most common reported emergency and it is likely that some of these episodes relate to hypoglycemia [63].

Assistance at airports and in aircrafts

Emergency medical assistance is available at most domestic and international airports and is under control of the airport operator. As per the "Policies and Recommended Practices Handbook, 2009, Seventh Edition", emergency medical services should be provided to passengers and other personnel, in addition to supportive medical facilities. This includes emergency rescue, on-field care and stabilization, care during transit and transfer to definitive care in the nearest hospital, if the need arises.

In case of any emergency on board, the airline staff can call for a doctor/medical practitioner who is on board the flight to volunteer [64]. In addition, it is imperative that airline staff have basic knowledge about hypoglycemia, its detection and management. In a consensus, the International Air Transport Association (IATA) and Aerospace Medical Association recommend that the emergency medical kit (EMK) should contain, among other essential medications and equipment, 50% dextrose for intravenous use [65]. Ideally, EMK should contain a glucometer with strips, which would help to rule out hypoglycemia in any unconscious individual. However, glucometers do not feature in standard EMK although they are included in the enhanced EMK by some airlines [65]. An over-head announcement can be made requesting other passengers for a glucometer.

Hydration

It is important to maintain good hydration during long flights because the risk of dehydration is higher due to lower humidity and lower cabin pressure. The individual should be encouraged to take non-alcoholic and non-caffeinated beverages which do not contain refined carbohydrates.

Avoiding jetlag

Another issue when crossing time zones is the shift in day-night rhythm, altered sleep-wake cycle and the resultant jet lag. Jet lag refers to a constellation of symptoms including fatigue, sleep disturbances, low mood, reduced appetite and gastrointestinal disturbances, and reduced cognitive skills as well as psychomotor coordination. [66]. Jet lag is more likely to occur in those who travel across ≥5 time zones, especially when flying east. While jet lag can worsen affective disorders, it can also influence overall well-being and metabolic control. Adequate sleep before commencing on the trip, avoiding alcohol or caffeinated drinks, eating regular balanced meals as per local timings, maintaining physical activity and staying active during daylight hours can help minimize jet lag [40].

Melatonin, secreted by the pineal gland in response to darkness, regulates circadian rhythm. Circadian rhythm disturbances are associated with altered melatonin secretion [66]. Melatonin can reset circadian rhythm, alleviate symptoms of jet lag and improve sleep quality. However, its effects on metabolic control, if any, are not known. Melatonin can be used for few days in those who travel across >7-8 time zones. Side effects are usually mild and include drowsiness and sedation. However, its safety has not been well-studied and it should be used with caution in those with seizure disorders or those on anticoagulants [67].

Physical activity

During long flights, there is an increased risk of deep vein thrombosis (DVT) aggravated by prolonged sitting. Patients should be instructed to walk up and down the aisle periodically and avoid sitting for long hours. Isometric exercises of the legs are also helpful [25]. Footwear worn during travel should be comfortable with socks that do not cause undue compression.

Many individuals travel for pilgrimage and it often involves walking barefoot in mosques, temples or gurudwaras, sometimes on hot marble or stone. This leads to increased risk of diabetic foot injuries and ulcers. In a study of Hajj pilgrims with diabetes, the occurrence of foot blisters incurred during pilgrimage was reported to be 31% [32]. In another observational study, 60 of the 197 Hajj pilgrims had diabetes; 34% reported blisters and 25% had erythema resulting from barefoot walking [33]. Therefore, it is important to instruct patients on appropriate foot care and use of protective footwear at all times.

In addition, pilgrimage may involve increased risk of suboptimal glycemic control, dehydration and acute complications. The rate of hospital admissions in people with diabetes during Hajj was reported as 8.5%, of which 7.1% were episodes of ketoacidosis, 0.7% hypoglycemia and 0.7% uncontrolled diabetes [29]. Pilgrimage is often associated with travel and lodging in crowded spaces, exposure to extreme temperatures and insanitary conditions, thereby increasing the risk of respiratory and gastrointestinal infections.[19]Pre-travel counseling should include assessment of risk and advice regarding diet, strict adherence to treatment, frequent SMBG, hypoglycemia care, foot care and sick-day rules [30-31].

Some individuals such as young adults with type 1 diabetes may wish to engage in activities such as trekking at high altitudes. While such activities increase energy expenditure, they can also result in increased secretion of counter-regulatory hormones. Fitness for such activities should be assessed. There is a need for frequent SMBG, ensuring adequate hydration and planning of appropriate meals. The individual should also be made aware that meters may be inaccurate at high altitudes and insulin may be exposed to heat [41,46-47]. Therefore, insulin and other supplies should be packed with appropriate insulation.

Vaccinations and infections

Travelers should be instructed to check the recommended vaccination schedules of the countries being visited. It would be good practice to complete age-appropriate immunization schedules (such as those for measles, mumps, varicella, tetanus toxoid, and hepatitis B etc.) during a pre-travel visit as well as cover diseases that are specific to the regions being visited (such as hepatitis A, typhoid, yellow fever and meningococcal vaccines). Freedman et al published a comprehensive review on the epidemiology of vaccine-preventable diseases and appropriate vaccination in international travelers [68]. Individuals with diabetes, especially those who are ≥ 65 years age or with other comorbidities are candidates for influenza and pneumococcal vaccines.

Other health concerns that individuals with diabetes need to be aware of, especially when visiting tropical and subtropical countries include traveler's diarrhea, cholera, enteric fever, malaria, dengue fever, swine flu or more recently, COVID-19 infection. It is important to go through specific travel advisories and implement appropriate prevention strategies such as use of appropriate protective clothing, mosquito repellants, social distancing and face masks, and ensuring consumption of clean and hygienic water and food [37].

Strengths and limitations

There is a clear lack of published literature to guide persons with diabetes and their clinicians with respect to the management of diabetes during long-distance travel. This is a very genuine and valid issue that most patients encounter and most clinicians don't have clear answers to. Studies that have been conducted are observational and focus on the identification of challenges during travel. Till date, only one previous systematic review has been conducted by Pavela et al. [55] but it does not cover all aspects of care. We have reviewed existing literature and provide practical suggestions with regards to pre-travel assessment, packing for the journey, and strategies to manage diabetes during travel and stay abroad. Hence, this article is important in today's era when travel has become a very important part of life.

In this systematic review, most of the recommendations are based on logical empiricism since limited evidence is available from small observational studies. The suggestions on modification of insulin doses during long flights are based on good clinical sense and have not been validated in clinical studies. There is an urgent need for original work with regards to diabetes management during long-distance travel.

Conclusion

Safe flying with diabetes is all about carrying all relevant documents and prescriptions related to diabetes and other comorbidities; carrying all medications, insulin and related supplies much in excess of the treatment duration; maintaining the cold chain for transport and storage of insulin; increased frequency of self-monitoring of blood glucose during travel to guide treatment, minimize glycemic variability and avoid hypoglycemia, and ensure early detection and appropriate action in the event of hypoglycemia; maintaining hydration; and adjusting oral anti-diabetes medications and/or insulin dose based on the flight timings, meal timings and sleep timings.

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